

CLAIMS

What is claimed is:

1. An isolated polynucleotide that encodes a soluble cytokine receptor polypeptide comprising a sequence of amino acid residues that is at least 90% identical to the amino acid sequence as shown in SEQ ID NO:3, and

wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide sequence binds or antagonizes IL-TIF (SEQ ID NO:8).

2. An isolated polynucleotide according to claim 1, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a homodimeric receptor complex.

3. An isolated polynucleotide that encodes a soluble cytokine receptor polypeptide comprising a sequence of amino acid residues that is at least 90% identical to the amino acid sequence as shown in SEQ ID NO:3, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a heterodimeric or multimeric receptor complex.

4. An Isolated polynucleotide according to claim 3, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a heterodimeric or multimeric receptor complex further comprising a soluble Class I or Class II cytokine receptor.

5. An isolated polynucleotide according to claim 3, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a heterodimeric or multimeric receptor complex further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33) or a soluble IL-10 receptor polypeptide (SEQ ID NO:34), or a soluble DIRS1 receptor polypeptide (SEQ ID NO:35).

6. An isolated polynucleotide according to claim 3, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a heterodimeric or

multimeric receptor complex further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33) or a soluble IL-10 receptor polypeptide (SEQ ID NO:34), or a soluble DIRS1 receptor polypeptide (SEQ ID NO:35).

7. An isolated polynucleotide that encodes a soluble cytokine receptor polypeptide comprising a sequence of amino acid residues as shown in SEQ ID NO:3, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a heterodimeric or multimeric receptor complex.

8. An Isolated polynucleotide according to claim 7, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide further comprises a soluble Class I or Class II cytokine receptor.

9. An isolated polynucleotide according to claim 7, wherein the soluble cytokine receptor polypeptide encoded by the polynucleotide forms a heterodimeric or multimeric receptor complex further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33) or a soluble IL-10 receptor polypeptide (SEQ ID NO:34), or a soluble DIRS1 receptor polypeptide (SEQ ID NO:35).

10. An isolated polynucleotide according to claim 7, wherein the soluble cytokine receptor polypeptide further encodes an intracellular domain..

11. An isolated polynucleotide according to claim 3, wherein the soluble cytokine receptor polypeptide further comprises an affinity tag.

12. An expression vector comprising the following operably linked elements:

(a) a transcription promoter; a first DNA segment encoding a soluble cytokine receptor polypeptide having an amino acid sequence as shown in SEQ ID NO:3; and a transcription terminator; and

(b) a second transcription promoter; a second DNA segment encoding a soluble Class I or Class II cytokine receptor polypeptide; and a transcription terminator; and

wherein the first and second DNA segments are contained within a single expression vector or are contained within independent expression vectors.

13. An expression vector according to claim 12, further comprising a secretory signal sequence operably linked to the first and second DNA segments.

14. An expression vector according to claim 12, wherein the second DNA segment encodes a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33) or a soluble IL-10 receptor polypeptide (SEQ ID NO:34), or a soluble DIRS1 receptor polypeptide (SEQ ID NO:35).

15. A cultured cell comprising an expression vector according to claim 12, wherein the cell expresses the polypeptides encoded by the DNA segments.

16. A cultured cell comprising an expression vector according to claim 12, wherein the first and second DNA segments are located on independent expression vectors and are co-transfected into the cell, and cell expresses the polypeptides encoded by the DNA segments.

17. A cultured cell into which has been introduced an expression vector according to claim 12, wherein the cell expresses a heterodimeric or multimeric soluble receptor polypeptide encoded by the DNA segments.

18. A cell according to claim 15, wherein the cell secretes a soluble cytokine receptor polypeptide heterodimer or multimeric complex.

19. A cell according to claim 15, wherein the cell secretes a soluble cytokine receptor polypeptide heterodimer or multimeric complex that binds IL-TIF or antagonizes IL-TIF activity.

20. A DNA construct encoding a fusion protein comprising:
a first DNA segment encoding a polypeptide having a sequence of amino acid residues as shown in SEQ ID NO:3; and

at least one other DNA segment encoding a soluble Class I or Class II cytokine receptor polypeptide,

wherein the first and other DNA segments are connected in-frame; and

wherein the first and other DNA segments encode the fusion protein.

21. A DNA construct encoding a fusion protein according to claim 20, wherein at least one other DNA segment encodes a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33) or a soluble IL-10 receptor polypeptide (SEQ ID NO:34), or a soluble DIRS1 receptor polypeptide (SEQ ID NO:35).

22. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA construct encoding a fusion protein according to claim 20; and

a transcription terminator,

wherein the promoter is operably linked to the DNA construct, and the DNA construct is operably linked to the transcription terminator.

23. A cultured cell comprising an expression vector according to claim 22, wherein the cell expresses a polypeptide encoded by the DNA construct.

24. A method of producing a fusion protein comprising:

culturing a cell according to claim 23; and

isolating the polypeptide produced by the cell.

25. An isolated soluble cytokine receptor polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence as shown in SEQ ID NO:3, and

wherein the soluble cytokine receptor polypeptide binds IL-TIF or antagonizes IL-TIF activity.

26. An isolated polypeptide according to claim 25, wherein the soluble cytokine receptor polypeptide forms a homodimeric receptor complex.

27. An isolated polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence as shown in SEQ ID NO:3, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex.

28. An isolated polypeptide according to claim 27, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex further comprising a soluble Class I or Class II cytokine receptor.

29. An isolated polypeptide according to claim 27, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33) or a soluble IL-10 receptor polypeptide (SEQ ID NO:34), or a soluble DIRS1 receptor polypeptide (SEQ ID NO:35).

30. An isolated polypeptide according to claim 27, wherein the polypeptide forms a heterodimeric or multimeric receptor complex further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33) or a soluble IL-10 receptor polypeptide (SEQ ID NO:34), or a soluble DIRS1 receptor polypeptide (SEQ ID NO:35).

31. An isolated soluble cytokine receptor polypeptide comprising a sequence of amino acid residues as shown in SEQ ID NO:3, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex.

32. An isolated polypeptide according to claim 31, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex further comprising a soluble Class I or Class II cytokine receptor.

33. An isolated polypeptide according to claim 31, wherein the soluble cytokine receptor polypeptide forms a heterodimeric or multimeric receptor complex comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33) or a soluble IL-10

receptor polypeptide (SEQ ID NO:34), or a soluble DIRS1 receptor polypeptide (SEQ ID NO:35).

34. An isolated polypeptide according to claim 31, wherein the soluble cytokine receptor polypeptide further comprises an affinity tag, chemical moiety, toxin, or label.

35. An isolated heterodimeric or multimeric soluble receptor complex comprising soluble receptor subunits, wherein at least one of soluble receptor subunits comprises a soluble cytokine receptor polypeptide comprising a sequence of amino acid residues as shown in SEQ ID NO:3.

36. An isolated heterodimeric or multimeric soluble receptor complex according to claim 35, further comprising a soluble Class I or Class II cytokine receptor polypeptide.

37. An isolated heterodimeric or multimeric soluble receptor complex according to claim 35, further comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33) or a soluble IL-10 receptor polypeptide (SEQ ID NO:34), or a soluble DIRS1 receptor polypeptide (SEQ ID NO:35).

38. A method of producing a soluble cytokine receptor polypeptide that forms a heterodimeric or multimeric complex comprising:
culturing a cell according to claim 15; and
isolating the soluble receptor polypeptides produced by the cell.

39. A method of producing an antibody to soluble cytokine receptor polypeptide comprising:
inoculating an animal with a soluble cytokine receptor polypeptide selected from the group consisting of:
(a) a polypeptide comprising a homodimeric soluble cytokine receptor complex;
(b) a polypeptide comprising a soluble cytokine receptor heterodimeric or multimeric receptor complex comprising a soluble Class I or Class II cytokine receptor polypeptide;

(c) a polypeptide comprising a soluble cytokine receptor heterodimeric or multimeric receptor complex comprising a soluble CRF2-4 receptor polypeptide (SEQ ID NO:33);

(d) a polypeptide comprising a soluble cytokine receptor heterodimeric or multimeric receptor complex comprising a soluble IL-10 receptor polypeptide (SEQ ID NO:34);

(e) a polypeptide comprising a soluble cytokine receptor heterodimeric or multimeric receptor complex comprising a soluble DIRS1 receptor polypeptide (SEQ ID NO:35); and

wherein the polypeptide elicits an immune response in the animal to produce the antibody; and

isolating the antibody from the animal.

40. An antibody produced by the method of claim 39, which specifically binds to a homodimeric, heterodimeric or multimeric receptor complex comprising a soluble cytokine receptor polypeptide.

41. The antibody of claim 40, wherein the antibody is a monoclonal antibody.

42. An antibody which specifically binds to a homodimeric, heterodimeric or multimeric receptor complex according to claim 35.

43. A method for inhibiting IL-TIF-induced proliferation of hematopoietic cells and hematopoietic cell progenitors comprising culturing bone marrow or peripheral blood cells with a composition comprising an amount of soluble cytokine receptor sufficient to reduce proliferation of the hematopoietic cells in the bone marrow or peripheral blood cells as compared to bone marrow or peripheral blood cells cultured in the absence of soluble cytokine receptor.

44. The method of claim 43, wherein the hematopoietic cells and hematopoietic progenitor cells are lymphoid cells.

45. The method of claim 44, wherein the lymphoid cells are macrophages or T cells.

46. A method of reducing IL-TIF-induced or IL-9 induced inflammation comprising administering to a mammal with inflammation an amount of a composition of soluble cytokine receptor sufficient to reduce inflammation.

47. A method of suppressing an immune response in a mammal exposed to an antigen or pathogen comprising:

- (1) determining a level of an antigen- or pathogen-specific antibody;
- (2) administering a composition comprising soluble cytokine receptor polypeptide in an acceptable pharmaceutical vehicle;
- (3) determining a post administration level of antigen- or pathogen-specific antibody;
- (4) comparing the level of antibody in step (1) to the level of antibody in step (3), wherein a lack of increase or a decrease in antibody level is indicative of suppressing an immune response.